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(088802-8704)

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**REMARKS**

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The present invention relates to co-repressor polypeptides that are capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Exemplary members of the silencing mediators of retinoic acid and thyroid hormone receptors (SMRT) family of co-repressors are provided, including full length human SMRT co-repressors, as well as various isoforms of mouse and *Drosophila* SMRT co-repressors.

By the present communication, claims 3-5, 14, 23, and 25 have been amended to define Applicants' invention with greater particularity. In view of these amendments, claim 24 has been cancelled. No new matter is introduced by the subject amendments as the amended claim language is fully supported by the specification and original claims.

In view of the amendments submitted herewith, claims 3-5, 14, 16, 18-23, and 25 remain pending in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination, is presented in the Listing of Claims, beginning on page 2 of this communication, with an appropriate status identifier for each claim.

**Rejections under 35 U.S.C. §102**

The rejection of claims 3-5, 19-22 under 35 U.S.C. §102(b) as allegedly being anticipated by Chen et al. (Nature, October 1995, vol. 377(6548), pp. 454-457), is respectfully traversed. In particular, Applicants respectfully disagree with the Examiner's assertion that "the polypeptide taught by Chen is encoded by a polynucleotide sequence that encodes a polypeptide that is ~94% identical to the sequence of SEQ ID NO:5" (Office Action, page 6). The Examiner cites the alignment found in Exhibit A, result #6 of the Office Action mailed May 23, 2005 in support of this assertion. However, the 94% identity appears to reflect a local percent identity rather than a global percent identity. Such a local alignment disregards the substantial number of additional residues (i.e., 1,030 residues) provided by SEQ ID NO:5. It is respectfully submitted that a

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global alignment of the full length sequences of SEQ ID NO:5 and the Chen polypeptide represents the appropriate means of determining the relevant percent identity between the two sequences. Such a global alignment was performed by clustalw analysis (see attached alignment). This alignment suggests that the two sequences have approximately only 60% identity. Thus, the Chen polypeptide does not meet the "at least 80% sequence identity to SEQ ID NO:5" requirement of claim 4. Therefore, the Chen reference does not anticipate the present claims.

Accordingly, reconsideration and withdrawal of this rejection of claims 3-5 and 19-22 under 35 U.S.C. §102(b) are respectfully requested.

The rejection of claims 3-5, 14, and 19-22 under 35 U.S.C. §102(a) as allegedly being anticipated by Park et al. (PNAS USA, 30 March 1999, vol. 96(7), pp. 3519-3524), is respectfully traversed at least for the reasons already of record. Specifically, Park et al. merely published findings similar to those reported by Applicants in Ordentlich et al (PNAS 96(6):2639-44), two weeks after the publication of the Ordentlich reference. The earlier publication by Ordentlich of the claimed extended isoform of SMRT clearly demonstrates that Applicants were in possession of the present invention before the effective date of the Park publication. Thus, the Park reference is not applicable against the present claims.

However, in efforts to reduce the issues and expedite prosecution, claim 4 has been amended to recite "the amino acid sequence of SEQ ID NO: 5 or conservative variations thereof." The sequence disclosed by Park contains deletions and additions, relative to SEQ ID NO:5. Such differences are not regarded as "conservative variations" and therefore, this sequence does not satisfy this requirement of claim 4. Thus, this reference does not anticipate the claims at issue.

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Accordingly, reconsideration and withdrawal of this rejection of claims 4, 19 and 21-22 under 35 U.S.C. §102(a) are respectfully requested.

The rejection of claims 23 and 25 under 35 U.S.C. §102(a) as allegedly being anticipated by GenBank Accession No. NM\_002900.1 (GenBank ID No. g4506452, March 19, 1999), is respectfully traversed. However, in efforts to reduce the issues and expedite prosecution, claim 23 is amended herein to require that embraced oligonucleotides encode at least 5 amino acid residues of specific portions of SEQ ID NO:5, 7, or 9. Such oligonucleotides would not be expected to hybridize to the sequence of GenBank Accession No. NM\_002900.1.

Accordingly, reconsideration and withdrawal of this rejection of claims 23 and 25 under 35 U.S.C. §102(a) are respectfully requested.

*Rejections under 35 U.S.C. §112, first paragraph—Written description*

The rejection of claims 23-25 under 35 U.S.C. §112, first paragraph as allegedly containing new matter, is respectfully traversed.

In particular, Applicants disagree with the Examiner's assertion, with respect to the term 'suitable stringency conditions,' that the specification "does not define these exact conditions and that the skilled artisan has no basis to visualize what these 'suitable' conditions might be" (Office Action, page 11). It is respectfully submitted that, given that DNA hybridization techniques well-known in the art, the skilled artisan could readily identify suitable hybridization conditions to achieve the desired hybridization to the recited sequences. However, in efforts to reduce the issues and expedite prosecution, the phrase "suitable stringency conditions" has been amended herein to recite "high stringency conditions."

Applicants further disagree with the Examiner's assertion that the specification allegedly provides no support for the requirement in claim 23 that embraced oligonucleotides do not hybridize to "a polynucleotide encoding an amino acid sequence consisting of amino acids 1031

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to 2517 of SEQ ID NO:5." However, in efforts to reduce the issues and expedite prosecution, the language at issue has been deleted from the claim as amended herein.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

The further rejection of claims 23-25 under 35 U.S.C. §112, first paragraph as allegedly failing to satisfy the written description requirement with respect to the claimed genus of oligonucleotides, is respectfully traversed.

In particular Applicants respectfully disagree with the Examiner's assertion that "the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of oligonucleotides" (Office Action, page 15). Contrary to the Examiner's assertion, the skilled artisan could readily identify oligonucleotides that meet the requirements of the claims. For example, the skilled artisan could simply perform a multiple sequence alignment of the relevant sequences and readily identify those oligonucleotides that would be expected to hybridize to some sequences but not to others. However, in efforts to reduce the issues and expedite prosecution, claim 4 (from which claim 23 depends) and claim 23 have been amended herein to define Applicants' invention with greater particularity. For example, claim 4 has been amended to recite "the amino acid sequence of SEQ ID NO: 5 or conservative variations thereof." Claim 23 has been amended to require that embraced oligonucleotides encode at least 5 amino acid residues of specific portions of SEQ ID NO:5, 7, or 9.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph—Enablement

The rejection of claims 14 and 16 under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement, is respectfully traversed. Applicants

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respectfully disagree with the Examiner's assertion that "[t]he specification does not enable any person skilled in the art to which it pertains, or with which is most nearly connected, to make and use the invention commensurate in scope with these claims" (Office Action, page 15). Contrary to the Examiner's assertion, the claims are fully enabled.

The Examiner acknowledges that the specification is "enabling for polynucleotides encoding a SMRT co-repressor, where the polynucleotide comprises a sequence having at least 80% identity with nucleotides 1 to 3094 of SEQ ID NO:4" (Office Action, page 15). However, the Examiner asserts that the specification "does not reasonably provide enablement for complements of these sequences, which also must encode a SMRT co-repressor" (Office Action, page 15). Applicants respectfully disagree with the Examiner's assertion. It is respectfully submitted that one of skill in the art would not have interpreted the claim as requiring that the complement encode a SMRT co-repressor. However, in efforts to reduce the issues and expedite prosecution, claim 14 has been rewritten to explicitly define the complement as would be readily understood by one of skill in the art, i.e., as a sequence complementary to the sequence encoding a SMRT co-repressor.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

35 U.S.C. §112, second paragraph

The rejection of claims 3, 14, 16, and 23-25 under 35 U.S.C. §112, second paragraph as allegedly being indefinite, is respectfully traversed.

Specifically with respect to claim 3, Applicants respectfully disagree with the Examiner's assertion that "the metes and bounds of the term 'less than about' are unclear" (Office Action, page 18). Contrary to the Examiner's assertion, this claim is clear as written. However, in order to reduce the issues and expedite prosecution, the phrase at issue has been amended to read "less than."

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With respect to claims 14 and 16, Applicants respectfully disagree with the Examiner's assertion that "[i]t is unclear how the polynucleotides of part (b) can encode a SMRT co-repressor, or portion thereof, when they are complementary to sequences in part (a) that actually do encode an SMRT co-repressor" (Office Action, page 19). Contrary to the Examiner's assertion, these claims are clear as written. However, in efforts to reduce the issues and expedite prosecution, these claims have each been amended to make it abundantly clear that the claimed polynucleotide embraces both the coding sequence of (a) and complement thereto in (b). Thus, the nucleotide of part (b) of the claim would not be required to encode a SMRT co-repressor. Furthermore, with respect to the Examiner's assertion that the phrase "provided that the polynucleotide does not contain a sequence identical to SEQ ID NO:11" is allegedly indefinite in that it is allegedly unclear if the phrase refers to the polynucleotide encoding SMRT or the complement thereof, this phrase has been incorporated into part (a).

With respect to claims 23-25, Applicants respectfully disagree with the Examiner's assertion that these claims are allegedly "vague and indefinite in that the metes and bounds of the phrase 'suitable stringency conditions' are unclear" (Office Action, page 19). It is respectfully submitted that one of skill in the art could readily identify "suitable" hybridization conditions in order to achieve hybridization of the oligonucleotide to the recited polynucleotide sequences. However, in efforts to reduce the issues and expedite prosecution, this phrase has been amended herein to recite "high" stringency conditions.

With respect to claim 24, Applicants respectfully disagree with the Examiner's assertion that "the metes and bounds of the phrase 'wherein the polynucleotide encodes at least five contiguous amino acids' ... are unclear" (Office Action, page 20). The Examiner further asserts that it is allegedly unclear which polynucleotide "encodes at least five contiguous amino acids" (Office Action, page 20). Contrary to the Examiner's assertion, this claim is clear as written. However, in efforts to reduce the issues and expedite prosecution, the phrase at issue has been

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amended to recite "wherein the oligonucleotide encodes at least five contiguous amino acids" to further clarify the polynucleotide to which the phrase refers.

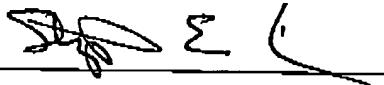
Accordingly, reconsideration and withdrawal of this rejection of claims 3, 14, 16, and 23-25 under 35 U.S.C. §112, second paragraph, are respectfully requested.

### CONCLUSION

In view of the above amendments remarks, it is respectfully submitted that the present application is now in condition for allowance. Accordingly, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: December 20, 2006

By 

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Attachment: Alignment by Clustalw of SEQ ID NO:5 and the Chen sequence

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